

UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.: 10/779,828
Applicant: Sudhir R. Brahmhatt
Filed: February 17, 2004
Title: OXYGEN-ASSISTED FERMENTATION PROCESS
TC/A.U.: 1651
Examiner: Deborah K. Ware
Confirmation No.: 9145
Docket No.: MG US 1
Customer No.: 000040582

Commissioner for Patents
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APPELLANT'S REPLY BRIEF

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Sir:

This Brief is filed in response to the Examiner's Answer dated January 17, 2008.

APPLICANT'S REMARKS TO EXAMINER'S ANSWER

The following remarks are in response to the Examiner's comments set forth in section "(9) Grounds for Rejection" at page and section "(10) Response to Argument" at pages 3-14 of the Examiner's Answer. These remarks are further intended to supplement the arguments set forth in the Appellant's Brief.

Motivations Cited By the Examiner

As the explicitly recited motivations for combining the teachings of EP 0 341 878 A1 with each of the Cheng references, the Examiner states that

"It would have been obvious ... to replace the air in each of the Cheng references with the inert gas disclosed by EP ... because the inert gas of EP would have been expected to mix but not react with the secondary gas disclosed by each of the Cheng references, and increased efficiency obtained from its continuous injection into the fermenter as disclosed by EP would have been an obvious modification.

(first ¶ of page 5). Applicant respectfully asserts that the first recited motivation, "mix but not react", is not sufficient. One of ordinary skill in the art would have found that a plethora of gases would have been expected to mix but not react with secondary gas disclosed by the Cheng references, such as argon, carbon dioxide, helium, krypton, neon, nitrogen, or xenon. These gas properties are not properly affirmative reasons for selecting a gas. Rather, a gas's lack of these properties is more of a reason not to select that gas. Thus, this is nothing more than an attempt to say that a modification is desirable simply because it would not have an immediately recognizable disadvantage.

Applicant also respectfully argues that the second recited motivation, "increased efficiency", is not sufficient because one of ordinary skill in the art would not have had a reasonable expectation of success in duplicating such "increased efficiency" in modifying the Cheng references with the teachings of the EP reference in the manner suggested by the Examiner.

The Supreme Court has held that "[I]f a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it

would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill.” *KSR Int’l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740, 82 USPQ2d 1385, 1396 (2007). The operative question in this “functional approach” is thus “whether the improvement is more than the predictable use of prior art elements according to their established functions, *Id.* at 1740, 82 USPQ2d at 1396. The answer to this operative question is that the claimed subject matter is indeed more than the predictable use of prior art elements according to their established functions because one of ordinary skill in the art would have recognized that the performance of the prior art elements relied upon by the examiner would likely have not been predictable and thus would have had no reasonable expectation of success.

Appellant notes that the Examiner’s showing of “increased efficiency” is in reference to a base case of agitation provided by an impeller (“Agitation/aeration operation alone” vs. “Pumped loop operation” on page 5 of EP reference). However, one of ordinary skill in the art would not have had a reasonable expectation of success in duplicating such efficiency in the hypothetical combination of the Cheng and EP references. This is because the Cheng references on one hand, and the EP reference on the other hand, operate in significantly different ways. The EP reference utilizes an impeller to provide agitation of gases and culture media, an injector within the vessel to provide a CO₂-stripping gas (in the case of an inert gas), a pipe loop to oxygenate the culture, and a set of nozzles to return the culture back to the vessel in an upper portion thereof. On the other hand, the Cheng references do not utilize an impeller to provide agitation. Rather, such agitation is provided by the separate injections of air and oxygen. Such a means of agitation is inapposite that of the EP reference. Also, the Cheng references utilize a set of injectors within, and adjacent to a bottom of, the vessel to oxygenate an oxygen-depleted portion of the culture media in the vessel. Such a location is inapposite that of the EP nozzle. Given these significant differences, one of ordinary skill in the art would not have

had a reasonable expectation of success in duplicating the "increased efficiency" relied upon by the Examiner.

Not All of the Limitations Are Disclosed By the Hypothetical Combination

The result of such a hypothetical modification of the Cheng references with the teachings of the EP reference would not result in each and every limitation required by the claims, namely substantially pure oxygen stream being the only gas that is continuously injected into the vessel. Appellant respectfully asserts that one of the Examiner's statements in the Answer is factually incorrect:

*"The claims differ from the cited Cheng references in that oxygen is not the sole reactive gas and **continuous injection thereof into the vessel is not specifically disclosed**"*

(fifth ¶ of page 4). Rather, one of the differences is that the Cheng references fail to disclose, teach or suggest that the stream of substantially pure oxygen **is the only gas** that is injected continuously into the vessel. Because the EP reference explicitly states that the inert gas should be injected continuously into the vessel (page 3, lines 38-39), the hypothetical combinations of the Cheng references would have resulted in **two gases** being continuously injected into the vessel and not a stream of substantially pure oxygen being the only gas that is injected continuously into the vessel as required by the claims.

In a separate portion of the Answer (first ¶ of page 8), the Examiner notes Appellant's argument that in the proposed combination of the Cheng and EP references, a stream of substantially pure oxygen would not be the sole gas continuously injected into the vessel. In response to Appellant's argument, the Examiner states that

[S]ince there is no requirement for mixing an inert gas or air with the substantially pure oxygen, and its only purpose is to remove excess carbon dioxide produced during fermentation it would have been an obvious modification to merely add more pure oxygen to replace the carbon dioxide because the cited prior art combination makes clear the desire in the art to inject substantially pure oxygen during fermentation as the sole reactive gas for increasing productivity of the fermentation process."

Appellant respectfully submits that this counter-argument is not on point and does not address the missing claim limitation: the stream of substantially pure oxygen is the sole gas continuously injected into the vessel.

Apparent New Rejection

Appellant respectfully asserts that the above Examiner's statement regarding the issue of the missing claim limitation appears to be a new rejection of the claims over the Cheng and EP references under 35 U.S.C. §103(a). The Examiner now appears to argue that:

- i) the EP reference teaches the importance of substantially pure oxygen being the sole reactive gas,
- ii) any gas that does not react with oxygen can be substituted for the inert gas because the inert gas serves the purpose of stripping CO₂.
- iii) it would have been obvious to inject oxygen through each of the two sets of injectors in the Cheng vessels in light of the EP's teachings and because it is simpler to inject one gas rather than two gases.

(second ¶ of page 9 through page 10).

If Appellant has misstated the Examiner or incorrectly interprets the language in the Answer, he respectfully requests the Examiner to clarify her remarks.

Assuming the above interpretation is correct, Appellant notes that this is the first time such a rejection has been raised during prosecution. Nevertheless, this rejection is legally insufficient for at least two reasons. First, one of ordinary skill in the art would not have had a reasonable expectation of successfully modifying the Cheng references to provide for injection of substantially pure oxygen through both sets of injectors in the manner suggested by the Examiner. Second, such a modification would have frustrated the purpose of the Cheng references.

One of ordinary skill in the art would not have had a reasonable expectation of successfully modifying the Cheng references to provide for injection of substantially pure oxygen through both sets of injectors in the manner suggested

by the Examiner. The air injectors of Cheng are for the purpose of providing lift, and therefore, agitation of the culture media in the vessel. If oxygen were substituted for the air, the gas flow rate would either have to be reduced substantially in order to maintain the same total oxygen bill needed for fermentation (air contains about 78% nitrogen and about 21% oxygen), or a great excess of oxygen would be injected into the culture media. In the first case, the gas flow rate would have to be reduced by 80%. One of ordinary skill in the art would have recognized that the flow pattern of culture media through in the vessel achieved by air injection would be severely altered, and as a result, such a one could not reliably predict whether sufficient agitation would be present to carry out fermentation without a substantial decrease in efficiency. In the second case, the total oxygen bill would be vastly increased. Cheng C discloses that oxygen should be injected at a flow rate of 0.1 to 20 scf/L•hr while air should be 10-400 scf/L•hr. One of ordinary skill in the art would have recognized that a 5 to 4,000 fold increase in oxygen added to the culture would have had a highly unpredictable result and as such would not have had a reasonable expectation of success. Finally, any selection of an oxygen gas flow rate through the formerly-air injectors to a level in between the above two cases would have been equally unpredictable and fraught with undue experimentation.

Purpose of Cheng References Is Frustrated

Appellant has previously argued that substitution of the air injected in each of the Cheng references with the inert gas of the EP reference would frustrate the Cheng references' purposes because one of the previously oxygen-containing streams could no longer support fermentation.

The Examiner counters in the Answer that the Cheng references' purposes would not have been frustrated because "an inert gas would not be capable of reacting with the oxygen" (last ¶ of page 7). Again, this argument is simply nothing more than an attempt to say that a modification is desirable simply because it would not have an immediately recognizable disadvantage.

The Examiner also counters that the Cheng references teach the inferiority of results achieved by air vs. oxygen such that the use of substantially pure oxygen as the sole reactive gas is desirable. While this may be true for the set of Cheng injectors through which oxygen is injected, stretching this argument to either replace the air with an inert gas or pure oxygen is unwarranted. Appellant argues that one of ordinary skill in the art would not likely conclude that Cheng teaches the inferiority of any air injection. Indeed, this argument serves to stand Cheng upon its head.

The Examiner further counters that while Cheng may be silent with respect to some of the steps employed by the EP reference, the test of obviousness under the law is whether the substitution of the air of Cheng with the inert gas of EP reference would have been expected to provide success results. Appellant argues that this is not an accurate recitation of the current state of the law on obviousness. A review of the Graham and KSR opinions make this point clear. It is not the Appellant's duty to provide evidence of unexpected results when the Examiner has initially failed to provide a *prima facie* case, as is the situation at hand. In addition to the many reasons above why the Examiner has failed to satisfy the PTO burden, the rejections do not provide a legally sufficient *prima facie* case for three additional reasons.

First, one of ordinary skill in the art would not have had a reasonable expectation of success in modifying the Cheng references for the reasons set forth at page 4 of this Reply Brief.

Second one of ordinary skill in the art would not have had a reasonable expectation of success in modifying the Cheng references because the gas flow rates would have severely disrupted the expected performance of the Cheng methods due to the difference in oxygen content between air and an inert gas. The air injected by the other set of injectors in the Cheng references serves two functions. It provides agitation through lift. It also provides amounts of oxygen for fermentation in addition to that provided by the oxygen injectors. This is explicitly taught by Cheng B and C where it is stated that 75-25% of the oxygen needed for

fermentation is supplied by the air bubbles (Cheng C at col. 4, Ins. 37-40 and Cheng B at col. 4, Ins. 37-40). This is implicitly taught by Cheng A as well because one of ordinary skill in the art would have clearly recognized that oxygen from the air bubbles would have provided a substantial amount of the total oxygen bill needed for fermentation similar to the teachings of Cheng B and C. If the air in the Cheng references were to be substituted with inert gas, then the oxygen injected through the other set of injectors would have had to have been increased correspondingly by 33-300%. At a minimum, this would have required a greater gas flow through that other set of injectors thereby increasing the resistance to the flow of culture media traveling from the bottom peripheral region of the vessel toward the bottom central region of the vessel and thence upwards. At a maximum, this would have reversed the flow of culture media through the vessel. One of ordinary skill in the art would have recognized this problem. Faced with no ready solution in the EP and Cheng references to this problem, such a one would have had no reasonable expectation of successfully combining the references in the manner suggested by the Examiner.

Third, modification of the Cheng A reference with the teachings of the EP reference in the manner suggested by the Examiner would have defeated the purpose of the Cheng A injector design. The Cheng A reference strives to provide a solution to the problem of reduced gas flows realized in an injector when the gas being injected is switched from air to oxygen, with the amount of oxygen actually being injected into the vessel remaining the same (§ 17 of Cheng A). If Cheng A were to be modified according to the teachings of the EP reference in the manner suggested by the Examiner, it would have the result of increasing the oxygen flow through the injector by up to 33-300% as explained above. Thus, one of ordinary skill in the art would recognize that the full benefit of the Cheng A injector design would not longer be realized.

In view of the foregoing it is submitted that the rejections of claims 1, 3-6, and 25-26 are improper and should be reversed.

Application No. 10/765,468
Amendment dated April 17, 2008
Reply to Office Action of November 08, 2006

Respectfully submitted,

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